

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) A method of treating or ameliorating hypertension in an animal, including a human, comprising administering an effective amount of (A) a compound of the formula I:



wherein:

- a. Het is a five membered heterocycle having one ring nitrogen and one ring oxygen, wherein said Het is an isoxazole and is not a dihydro or tetrahydro analog thereof;
- b. Het can be substituted on carbon atoms with
 1. one or more substituents independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C₁-C₃)alkylenedioxy, allyl, amino, ω -alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), cycloalkyl, dialkylamino, halo, hydroxy, (C₂-C₆)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylthio, alkylsulfonyl, alkylsulfinyl, alkylsulfonamido, and trifluoromethyl, ~~morpholin-4-yl, 4-[C₆-or C₁₀]aryl, piperidin-1-yl, 4-[C₆-or C₁₀]aryl, piperazin-1-yl, thiomorpholin-4-yl, piperidin-1-yl, Ar*~~ {wherein, consistent with the rules of aromaticity, Ar* is C₆-or C₁₀-aryl or a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring can be optionally fused to a substituted benzene, pyridine, pyrimidine, pyridazine, pyrazine, or (1,2,3)triazine (wherein the ring fusion is at a carbon-carbon double bond of Het)}, Ar* alkyl, Ar* O, Ar*SO₂, Ar*SO, Ar*S, Ar*SO₂NH, Ar*NH, (N-Ar*)(N-alkyl)N, Ar*C(O), Ar*C(O)NH, Ar*NH-C(O), and (N-Ar*)(N-alkyl)N-C(O)-; or
 2. two adjacent substitutions together with their ring carbons form a fused C₆ or C₁₀ aryl ring which aryl ring can be substituted as set forth below; or

3. two adjacent substitutions together with their ring carbons form a C₅-C₇ fused cycloalkyl ring having up to two double bonds including any fused double bond of the Het group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxy, carbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo; or

4. two adjacent substitutions together with their ring carbons form a fused 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N; or

5. two adjacent substitutions together with their ring carbons form a fused five to eight membered fused heterocycle, wherein the ring fusion is at a carbon-carbon bond of Het, wherein the fused heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, sulfur, or S(O)_n, wherein S(O)_n is 1 or 2; and

c. Het can be substituted on the ring nitrogen atoms atoms with

~~1. —hydrogen, alkyl, alkoxy, carbonylalkyl, Ar*, Ar*alkyl, Ar*C(O)alkyl, ArS*(O)alkyl, Ar*S(O)₂alkyl, so long as the ring nitrogen atoms are not quaternized;~~

~~2. 1.~~ amino; or

~~3. 2.~~ at most one nitrogen with oxido (-O) to form an N-oxide; and

d. Y is substituted on a ring carbon adjacent to the ring nitrogen and is hydrogen;

~~wherein aryl or Ar* in addition to any substitutions specifically noted can be substituted with one or more substituents selected from the group of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxy, carbonyl, alkoxy, carbonylalkyl, alkyl, alkylamino, (C₁-C₃)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω -alkylenesulfonic acid, alkylthio, allyl, amino, Ar*C(O), Ar*C(O)NH, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C₂-C₆)hydroxyalkyl, mercapto, nitro, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, Ar*O, Ar*, Ar*alkyl, sulfamoyl, sulfonic acid, 1-pyrrolidinyl, 4-[C₆-or-C₁₀]arylpiperidin-1-yl and 4-[C₆-or-C₁₀]arylpiperazin-1-yl; and~~

wherein heterocycles except those of Het or Ar*, can be substituted with, in addition to substitutions specifically noted, one or more substituents selected from acylamino, alkanoyl, alkoxy, alkoxy, carbonyl, alkoxy, carbonylalkyl, alkyl, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, Ar*C(O)-, Ar*O-, Ar*-, Ar*alkyl, wherein, consistent with the rules of aromaticity, Ar* is C₆ or C₁₀ aryl or a 5- or 6-membered heteroaryl ring, wherein the 6-

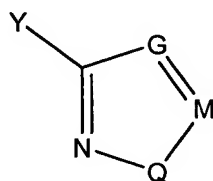
membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring can be optionally fused to a substituted benzene, pyridine, pyrimidine, pyridazine, pyrazine, or (1,2,3)triazine (wherein the ring fusion is at a carbon-carbon double bond of Het), carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, 4-[C₆ or C₁₀]arylpiperidin-1-yl, 4-[C₆ or C₁₀]arylpiperazin-1-yl, (C₁-C₃)alkylenedioxy, oxo, sulfamoyl, and trifluoromethyl; and

aryl or Ar* in addition to any substitutions specifically noted can be substituted with one or more substituents selected from the group of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C₁-C₃)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, Ar*C(O)-, Ar*C(O)NH-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C₂-C₆)hydroxyalkyl, mercapto, nitro, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, Ar*O-, Ar*-, Ar*-alkyl-, sulfamoyl, sulfonic acid, 1-pyrrolidinyl, 4-[C₆ or C₁₀]arylpiperidin-1-yl and 4-[C₆ or C₁₀]arylpiperazin-1-yl;

or a pharmaceutically acceptable salt of said compounds.

2. (Previously presented) The method of claim 1, wherein Het is a five membered heterocycle having one ring nitrogen and one ring oxygen, wherein said Het is an unsubstituted isoxazole or a pharmaceutically acceptable salt thereof.

3. (Currently amended) The method of claim 1, wherein Het-Y is



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wherein G, and M, are selected from the group consisting of C-R^h-and C-Rⁱ ;

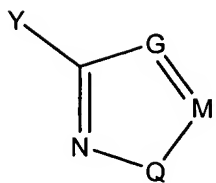
Q is O,

b. wherein R^h or Rⁱ are

- (1) independently selected from hydrogen, acylamino, ureido, thioureido, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C₁-C₃)alkylenedioxy, allyl, amino, ω-alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), cycloalkyl, dialkylamino, halo, hydroxy, (C₂-C₆)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylthio, alkylsulfonyl, alkylsulfinyl, alkylsulfonamido, trifluoromethyl, ~~morpholin-4-yl, 4-[C₆-or C₁₀]aryl piperidin-1-yl, 4-[C₆-or C₁₀]aryl piperazin-1-yl, thiomorpholin-4-yl, piperidin-1-yl, Ar*, Ar* alkyl, Ar* O, Ar*SO₂, Ar*SO, Ar*S, Ar*SO₂NH, Ar*NH, (N Ar*)(N alkyl)N, Ar*C(O), Ar*C(O)NH, Ar*NH C(O), and (N Ar*)(N alkyl)N C(O);~~
- (2) R^h and Rⁱ where adjacent, together with their ring carbons form a C₅-C₇ fused cycloalkyl ring having up to two double bonds including the fused double bond of the Het group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl-, alkoxycarbonyl-, amino-, aminocarbonyl-, carboxy-, fluoro-, or oxo-substituents, except in the case of alkyl, alkoxycarbonyl, and fluoro substituents, which can be located on the same or different carbon atoms;
- (3) R^h and Rⁱ where adjacent, together with their ring carbons form a fused C₆ or C₁₀ aryl ring;
- (4) R^h and Rⁱ where adjacent, together with their ring carbons form a fused five to eight membered fused heterocycle, wherein the ring fusion is at a carbon-carbon bond of Het, wherein the fused heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, sulfur, or S(O)_n, wherein S(O)_n is 1 or 2; or
- (5) R^h and Rⁱ where adjacent, together with their ring carbons form a fused 5- or 6-membered heteroaryl ring containing at least one and up to three atoms of N for the 6-membered fused heteroaryl rings and from one to three atoms of N or one atom of O or S and zero to two atoms of N for the 5-membered fused heteroaryl rings.

4. (canceled)

5. (Previously presented) The method of claim 3, wherein Het-Y is



wherein G is C-R^h;

M is C-Rⁱ; and

Q is O, S, or N-R^g.

6. – 10. (canceled)

11. (Currently amended) The method of claim 5, wherein Rⁱ is hydrogen and R^h is amino, Ar*, acylamino, ureido, or ~~thoureido~~ thioureido.